DOCKET NO.: ISIS-1169 Application No.: 08/117,363

Office Acti n Dated: August 29, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (Currently Amended). A compound comprising a plurality of linked nucleosides, wherein:

each nucleoside includes a pentofuranosyl sugar portion and a base portion; and at least one of said nucleosides bears at a 2'-O-position, a 3'-O-position, or a 5'-O-position a terminal substituent having formula:

$$-R_A - N(R_{1a})(R_{1b})$$

where:

R_A is alkyl having from 1 to about 10 carbon atoms or (CH₂-CH₂-Q)_x;

 R_{1a} and R_{1b} , independently, are H, R_2 , or an amine protecting group or have formula $C(X)-R_2$, $C(X)-R_A-R_2$, $C(X)-Q-R_A-R_2$, $C(X)-Q-R_2$; and

 R_2 is a folate, a steroid molecule, a reporter molecule, a lipophilic molecule, a reporter enzyme, a peptide, a protein, or has formula -Q-(CH₂CH₂-Q-)_x-R₃;

X is O or S;

each Q is, independently, is NH, O, or S;

x is about 1 to about 50;

 R_3 is H, R_A , C(O)OH, C(O)OR_A, C(O)R₄, R_A -N₃, or R_A -NH₂;

R₄ is Cl, Br, I, SO₂R₅ or has structure:

Page 3 of 11

DOCKET NO.: ISIS-1169 Application No.: 08/117,363

Office Action Dated: August 29, 2003

m is 2 to 7; and

R₅ alkyl having 1 to about 10 carbon atoms.

2 (Original). The compound of claim 1 wherein more than one of said nucleosides bear said substituent at a 2'-O-position, a 3'-O-position, or a 5'-O-position.

3 (Original). The compound of claim 1 wherein R_A is $(CH_2)_n$ where n is an integer from 1 to about 10.

4 (Original). The compound of claim 3 wherein n is 6.

5 (Original). The compound of claim 1 wherein said R_{1a} is H and R_{1b} , together, are phthalimido.

6 (Original). The compound of claim 1 wherein R_{1a} is H and R_{1b} is C(O)- $(CH_2)_n$ - R_2 where n is an integer from 1 to about 10.

7 (Original). The compound of claim 1 wherein R_{1a} is H and R_{1b} is R_2 .

DOCKET NO.: ISIS-1169 Application No.: 08/117,363

Office Action Dated: August 29, 2003

- 8 (Original). The compound of claim 1 wherein R_{1a} is H and R_{1b} is C(O)-O- R_2 .
- 9 (Original). The compound of claim 1 wherein R_{1a} and R_{1b} both are alkyl.
- 10 (Original). The compound of claim 1 wherein R_{1a} is H and R_{1b} is C(O)- $(CH_2)_n$ - R_2 where n is an integer from 1 to about 10.
 - 11 (Original). The compound of claim 10 wherein R_2 has formula -(CH_2)₅-NH-.
 - 12 (Original). The compound of claim 1 wherein R_{1a} is H and R_{1b} is C(S)-NH-R₂.
- 13 (Original). The compound of claim 1 wherein R_2 includes pyrene, fluorescein, dinitrophenyl, cholesterol, acridine.
 - 14 (Original). The compound of claim 1 wherein R_{1a} is H and R_{1b} is $C(O)-R_2$.
- 15 (Original). The compound of claim 14 wherein R_2 has formula -O-(CH₂CH₂-O-)_x- R_3 .

DOCKET NO.: ISIS-1169 Application No.: 08/117,363

Office Action Dated: August 29, 2003

16 (Currently Amended). A nucleoside comprising a pentofuranosyl sugar portion and a base portion, wherein said nucleoside bears at a 2'-O-position, a 3'-O-position, or a 5'-O-position a substituent having the formula:

$$-R_A - N(R_{1a})(R_{1b})$$

where:

R_A is alkyl having from 1 to about 10 carbon atoms;

 R_{1a} and R_{1b} , independently, are H, R_2 , or an amine protecting group or have formula $C(X)-R_2$, $C(X)-R_A-R_2$, $C(X)-Q-R_A-R_2$, $C(X)-Q-R_2$; and

 R_2 is a steroid molecule, a reporter molecule, a lipophilic molecule, a reporter enzyme, a peptide, a protein, or has formula $-Q-(CH_2CH_2-Q-)_x-R_3$;

X is O or S;

each Q is, independently, is NH, O, or S;

x is about 1 to about 50;

 R_3 is H, R_A , C(O)OH, C(O)OR_A, C(O)R₄, R_A -N₃, or R_A -NH₂; and

R₄ is Cl, Br, I, SO₂R₅ or has structure:

m is 2 to 7; and

R₅ alkyl having 1 to about 10 carbon atoms.

DOCKET NO.: ISIS-1169 Applicati n No.: 08/117,363

Office Action Dated: August 29, 2003

17 (Currently Amended). The nucleoside of claim 16 wherein R_A is $(CH_2)_n$ where n is an integer from 1 to about 10.

18 (Currently Amended). The nucleoside of claim 16 wherein n is 6.

19 (Currently Amended). The nucleoside of claim 16 wherein said R_{1a} is H and R_{1b} , together are phthalamido.

20 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} is H and R_{1b} is C(O)- $(CH_2)_n$ - R_2 where n is an integer from 1 to about 10.

21 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} is H and R_{1b} is R_2 .

22 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} is H and R_{1b} is C(O)-O- R_2 .

23 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} and R_{1b} both are alkyl.

DOCKET NO.: ISIS-1169 Application No.: 08/117,363

Office Action Dated: August 29, 2003

24 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} is H and R_{1b} is C(O)- $(CH_2)_n$ - R_2 where n is an integer from 1 to about 10.

25 (Currenly Amended). The nucleoside of claim 24 wherein R_2 has formula -(CH₂)₅-NH-.

26 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} is H and R_{1b} is C(S)-NH- R_2 .

27 (Currently Amended). The nucleoside of claim 16 wherein R₂ includes pyrene, fluorescein, dinitrophenyl, cholesterol, acridine.

28 (Currently Amended). The nucleoside of claim 16 wherein R_{1a} is H and R_{1b} is C(O)-R₂.

29 (Curerntly Amended). The nucleoside of claim 28 wherein R₂ has formula -O-(CH₂CH₂-O-)_x-R₃.

Claims 30-35 (Canceled).